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Emergency Calls for ADHD Medication Errors Up 299%, Researchers Say 1 Drug May Be Partly to Blame

A study published Monday in Pediatrics reported a threefold rise in calls to poison centers for attention-deficit/hyperactivity disorder, or ADHD, drug-related adverse events. A particularly sharp increase in calls beginning around 2009 coincides with the approval of guanfacine, marketed under the brand name Tenex.

By Angelo DePalma, Ph.D.

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A study published Monday in Pediatrics reported a 299% increase in calls to poison control centers related to therapeutic errors associated with treatments for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents age 20 or younger.

In a press release, study co-author Natalie Rine, Pharm.D., said increases in medication errors are consistent with the rise in ADHD diagnoses during the past two decades, "which is likely associated with an increase in the use of ADHD medications."

In other words more diagnoses mean more prescriptions, which lead to more errors.

However, the authors of the study also said that while the increase in ADHD diagnoses from 2000 to 2009 may explain the rise in prescriptions and calls for those years, they believe the sharp uptick beginning in 2009 likely had another cause: the U.S. Food and Drug Administration's approval of guanfacine, marketed under the brand name Tenex, to treat ADHD in kids.

The study's authors wrote:

> "The marked increase in guanfacine-related therapeutic errors observed in our study beginning in 2009 coincides with its FDA approval for ADHD treatment.

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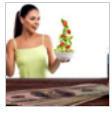
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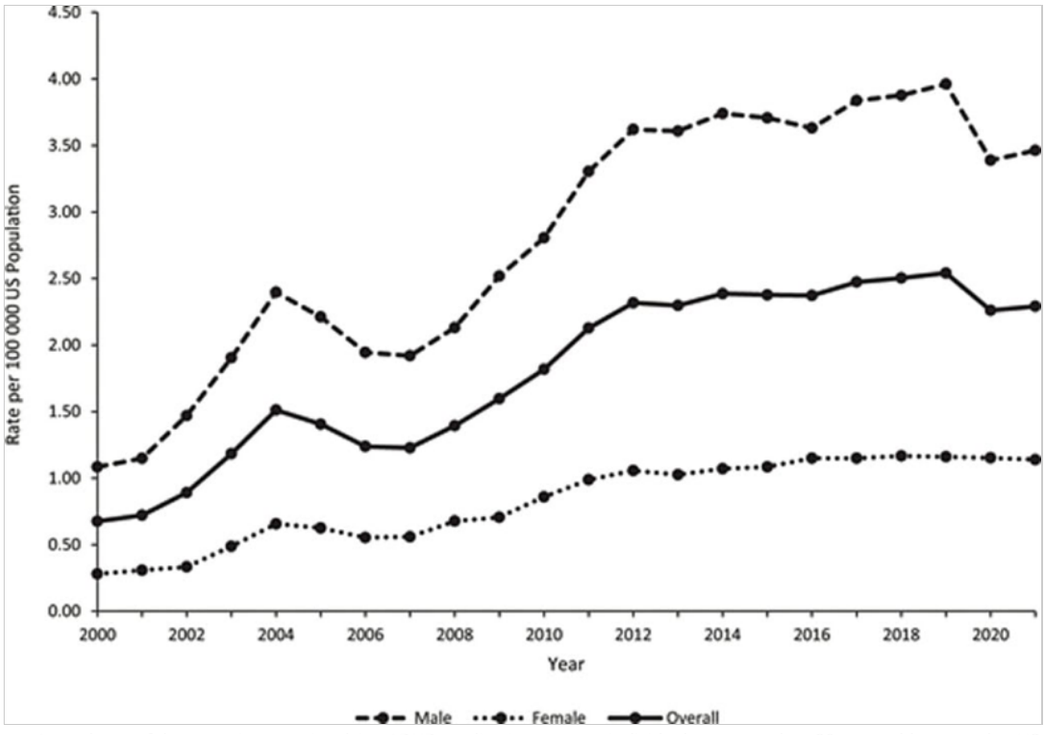
"In addition, the increases in serious medical outcomes and HCF [healthcare facility] admissions associated with ADHD medication-related therapeutic errors starting in 2009 were driven by guanfacine-related events."



Annual rate of therapeutic errors involving ADHD medications among individuals younger than 20 years old reported to US PCs by sex, National Poison Data System 2000 to 2021. Credit: Mikaela M. DeCoster, et al.

Figure 1 illustrates trends in poison center calls during the study period.

Although the FDA originally approved guanfacine for high blood pressure and not for ADHD, the drug received an endorsement from the American Academy for Child and Adolescent Psychiatry for use in children with ADHD in 2009, and full FDA approval to treat 6- to 17-year-old children with ADHD in 2010.

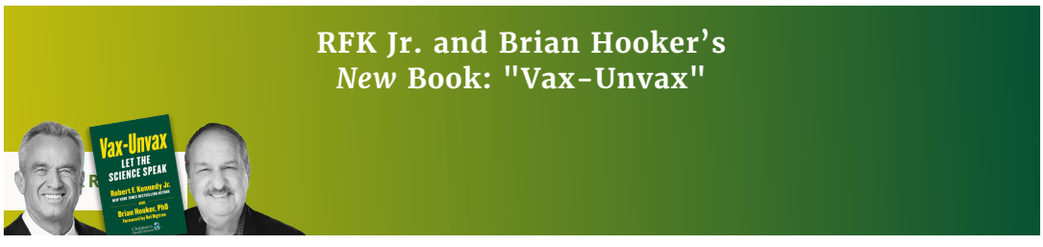
According to the study, therapeutic errors involving guanfacine were more likely to be clinically significant than for other ADHD medications, including stimulants.

Children who took guanfacine were more than five times as likely to be admitted to a hospital than those who took amphetamines or related drugs.

The authors attributed the higher admission rate in part to the drug's extended-release formulation, which spreads the drug's effect over a longer period of time than immediate-release medicines: An adverse event of moderate severity lasting 10 minutes may not trigger a call, but one continuing for an hour might.

ADHD is one of the most common pediatric neurodevelopmental disorders. A 2016 study reported that 6.1 million, or 9.4% of children ages 2-17 had received an ADHD diagnosis in their lifetimes, and 89% of those were still affected at the time of the report.

Approximately 3.3 million children — 5% of all U.S. kids — receive ADHD medication.



Children under 6 experienced twice as many serious outcomes

Researchers at Nationwide Children's Hospital, Columbus, Ohio — led by Gary A. Smith, M.D., Dr.PH. — examined both the characteristics of calls and their rising frequency.

They found the number of calls to poison centers for ADHD-related medications increased from 1,906 in 2000, to 5,235 in 2021, with an average of 3,985 calls per year and 87,691 total calls.

Only 17% of cases necessitated treatment but 2.3% required hospitalization (including 0.8% to a critical care unit).

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Overall, 4.2% of cases resulted in a serious medical outcome that included agitation, tremors, seizures or changes in mental status.

Children under 6 experienced twice as many serious outcomes and were hospitalized at three times the rate of 6-19-year-olds.

Males and children ages 6-12 accounted for 76% and 67% of all calls, with 93% of adverse events occurring at home.

In 54% of cases requiring calls, the person took two doses instead of one, and 26% of the time they took the wrong medicine.

The National Poison Data System (NPDS), the source of data for the study, defines therapeutic error as "an unintentional deviation from a proper therapeutic regimen that results in the wrong dose, incorrect route of administration, administration to the wrong person, or administration of the wrong substance."

A long list of drugs … and side effects

In addition to guanfacine, regulators have approved a wide variety of drugs to treat ADHD, most commonly the stimulants methylphenidate, amphetamine, lisdexamfetamine and modafinil, and the non-stimulants atomoxetine and clonidine.

Stimulants, which have an immediate and profound effect on ADHD symptoms, are considered first-line treatments. Side effects of these drugs include lack of appetite, weight loss, delayed growth, sleep disturbances, developmental delays and anxiety.

Doctors often prescribe non-stimulants when other conditions are present, for example tic disorders, or when stimulants might interfere with other medications a patient is taking.

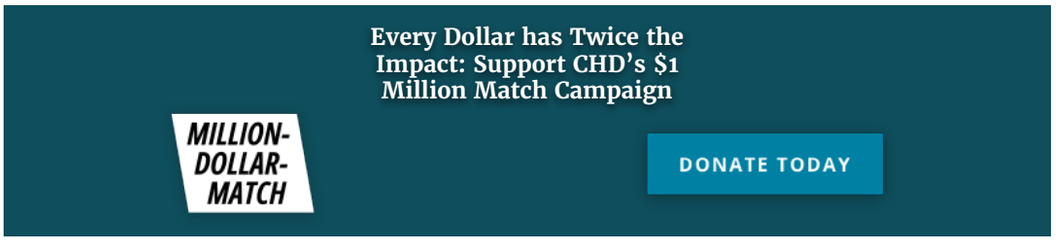
However not all experts agree that children with tics should avoid stimulants.

Unlike many other ADHD drugs, atomoxetine was specifically approved for that condition but carries a long list of serious side effects, including psychosis.

Guanfacine and clonidine were originally approved for lowering blood pressure in adults. Both drugs carry warnings for circulatory, metabolic and/or emotional disturbances.

Clonidine's original package insert does not inspire confidence in its use in children:

> "The frequency of CNS depression may be higher in children than adults. Large overdoses may result in reversible cardiac conduction defects or dysrhythmias, apnea, coma and seizures.
>
> "Signs and symptoms of overdose generally occur within 30 minutes to two hours after exposure. As little as 0.1 mg of clonidine has produced signs of toxicity in children."



Under-reporting of mild cases may have affected study outcomes

The authors claimed their paper added to knowledge of ADHD treatment because earlier studies "broadly considered all pharmaceuticals" used by children, not specific ADHD drugs.

This point may be valid because most children with ADHD have at least one other health problem for which they may be taking drugs.

The study design acknowledged this by including only emergency calls for which an ADHD drug was deemed a "first-ranked substance." That means the ADHD medicine was judged by a certified poison specialist to be responsible for the adverse event.

The authors cited only under-reporting as a study weakness. Cases may have been missed, for example, due to under-reporting of mild cases, or lack of rigor in determining first-ranked status in cases where children were taking more than one drug.

One weakness the authors mentioned only in passing was the possible role of prescribers. They listed 1714 cases of "iatrogenic" cases in a table, and referred to those cases once in the text. Iatrogenic means "caused by healthcare providers" — a medical mistake.

But the table also lists 1,789 cases in which the wrong formulation or strength was given, and 459 instances of "Confused unit of measure" — the confusion presumed to be on the part of the caregiver.

These are all caregiver mistakes. Added together, these 3,962 entries comprise 4.5% of all cases and would be the sixth-leading cause of drug reactions requiring an emergency call.

Also absent was discussion of the appropriateness of either drug type or dosage, diagnosis accuracy, length of treatment, adherence to prescribing instructions, whether doctors are prescribing either more ADHD drugs per patient or higher doses, or whether these drugs help in the long run.

ADHD symptoms persist into adulthood in about 80% of those diagnosed. An estimated 8.7 million adults in the U.S. are currently affected.

A market report by Credence Research estimates that worldwide sales of ADHD drugs will rise from $19.5 billion in 2020 to $34.8 billion in 2027. These medicines have been so successful financially, and unsuccessful therapeutically, that adults are now considered the "prime market" for what was once considered a childhood disease.

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Angelo DePalma, Ph.D.

Angelo DePalma, Ph.D., is a science reporter/editor for The Defender.

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Best Newest Oldest

Polly Green

7 days ago

Back when my kids were Dxed as ADHD (because autism was "infinitesimally rare!") back then, we were dispensed clonopin instead of clonidine and my son ended up in an ambulance. We thought about suing the grocery store pharmacy, and there was a lot of controversy about drug "mishaps" attributed to name similarities. Not long after, we decided to discontinue all medications. It wasn't worth it. The kids felt better as a result anyway.

11 0 Reply • Share ›

Gay Studebaker

7 days ago

Many parents of children diagnosed with ADHD don't realize how terrible processed foods are for these children. Autistic children as well. The chemicals and other ingredients like high fructose corn syrup have profoundly negative impact on everyone but especially children.

8 0 Reply • Share ›

Ektor
6 days ago

Another reason to avoid all drugs. Most of these things are not well tested or studied and put on the market purely to sell them and not to help anyone. The FDA is a criminal agency you do not want to trust with your good health or life.

6 0 Reply • Share ›

Jeremy Beckman
7 days ago

We weren't born with an amphetamine deficiency. Rather, certain people don't perform well in this society's 'metrics'. Also, highly processed food and their additives/colors can affect a child's developing mind, including hyperactive/inattentive behaviors. Long term stimulant use (of the amphetamine class especially) is not healthy for anyone's mind or body. It also squashes the creative/emotional sides of a developing child's brain while amplifying the logical reasoning side (which works rather well in the traditional school system). Worker robots that go insane down the line.

6 0 Reply • Share ›

Polly Green ↗ Jeremy Beckman
7 days ago

We finally were forced to conclude that the “hyperactivity” was really a kind of end-stage detoxification process, and the children were 13 and 15 anyway and were gradually getting better as they aged which points to a non-medical cause as well. I think back and wonder was it the introduction of glyphosate into the American diet which occurred a few years before? Was it the new requirement for flu shots in our county schools? It’s hard all these years later to know for certain. They’re in their thirties now.

6 0 Reply • Share ›

IamaproudAmerican
7 days ago

My youngest son was diagnosed with adhd years ago. He was given different drugs and none of them helped him. One caused him to have a rage episode which landed him in the hospital. We took him off all drugs and found a child psychologist who was part angel. He worked with my son for several years and it helped a lot. One of the things he taught him was lip reading. That helped him focus on what people said and he still uses it today.

5 0 Reply • Share ›

jann ↗ IamaproudAmerican
7 hours ago

Amazing! A psychiatrist who uses treatments other than drugs. The lip reading is brilliant! My son did various forms of neurofeedback, some of which require focusing on either a video or a picture forming and turning color on a screen. One was called "Heart Math." He improved tremendously in spelling and math with those.

0 0 Reply • Share ›

kris
6 days ago

When is it going to be standard procedure to advise an aluminum detox or a heavy metal detox for these kids? When will it be standard for doctors to check if there has been an environmental biological damage to the nervous system of these kids? Those pills are toxic!

It is a true crime that so many kids are given methamphetamine based drugs like Adderall or Ritalin in this country! Those also cause long term damage to the nervous system.

If you want to know why so many americans have an addiction to meth well look how many kids are prescribed meth based drugs by big pharma captured hospitals! That is not medicine!

4 0 Reply • Share ›

vgupta123
7 days ago

ADHD is probably a social disorder, not a mental one. In any case, it is best treated with counseling and drugless therapies.
Pharma keeps pushing psychiatric drugs with dubious benefits and serious harm. Children are especially vulnerable, and even when the drugs work, they are likely to become dependent on drugs for life--thus creating lifelong customers for pharma.

4 1 Reply • Share ›

kris ↗ vgupta123
6 days ago

I think it's mostly heavy metal poisoning and pesticides. Many kids are living in aluminum toxicity during their formative years due to all the aluminum adjuvants in the 'vaccines' -- these shots do not stay local in the shoulder or leg muscle and the adjuvants can bioaccumulate in the brain/ nervous system

When a poisonous snake bites someone in the muscle do we say oh don't worry it's the muscle so it will stay local? Why do they keep telling us the shots stay local?

5 0 Reply • Share ›

Deborah Mackay
5 days ago edited

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DIAGNOSE - LABEL - PRESCRIBE - REPEAT
PEOPLE DESTROYED & MURDERED
In 1988 when I was a young mother babysitting for neighbours. I lived in a row of 16 townhouses. Four of them, that I knew of, had children on Ritalin. That's 25% of the children in a row of townhouses. Appalled, I wrote our city newspaper column and called my write-up "Ritalin" a Teachers', Nurses' & Parents' Aid.

2 0 Reply • Share ›

J

jann

7 hours ago

When my son was young, I went to a couple of CHADD meetings. Two people presented, one for mental health and one for medication, at each meeting. I asked if they ever had an Occupational Therapist speak. I was told that "No, they only recommended what was proven medically." I then read that the maker of Ritalin had given a large donation to the organization. I also found out that Ritalin was known to cause heart attacks even though I was told by doctors and teachers that it was safe.

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